General

Guideline Title

A.S.P.E.N. clinical guidelines: support of pediatric patients with intestinal failure at risk of parenteral nutrition–associated liver disease.

Bibliographic Source(s)

Wales PW, Allen N, Worthington P, George D, Compher C, American Society for Parenteral and Enteral Nutrition, Teitelbaum D. A.S.P.E.N. clinical guidelines: support of pediatric patients with intestinal failure at risk of parenteral nutrition-associated liver disease. JPEN J Parenter Enteral Nutr. 2014 Jul;38(5):538-57. [71 references] PubMed

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Definitions for the grading of recommendations (Strong, Weak, Further research needed) and quality of evidence (High, Moderate, Low, Very Low) are provided at the end of the "Major Recommendations" field.

Is Ethanol Lock Effective in Preventing Bloodstream Infection and Catheter Removal in Children at Risk of Parenteral Nutrition–Associated Liver Disease (PNALD)?

A suggestion is made to use ethanol lock to prevent catheter-related bloodstream infections (CLABSI) and to reduce catheter replacements in children at risk of PNALD.

Evidence: Low and very low

Recommendation Grade: Weak

What Fat Emulsion Strategies Can Be Used in Pediatric Patients with Intestinal Failure to Reduce the Risk of or Treat PNALD?

Since the only intravenous (IV) fat emulsion available for use in the United States is soy-based fat emulsions (SOE), a suggestion is made to reduce the dose of SOE to ≤1 g/kg/d to treat cholestasis in children with PNALD. The quality of evidence supporting this recommendation is very low. Most studies are small observational studies. The desirable effect of reduction of liver indices has to be considered in light of the unknown effects of poor growth and development when lipids are restricted.

Evidence: Very Low

Recommendation Grade: Weak

Fish oil emulsion (FOE) is available in the United States under a compassionate use protocol. Until it is approved by the U.S. Food and Drug Administration (FDA), no recommendation can be made for use in the United States. The evidence supporting the use of FOE is very low quality. Included studies are small observational studies that are confounded by concurrent lipid dose reduction and advancement of enteral feedings. The desirable effect of improved cholestasis has to be considered in light of the unknown effects of poor growth and development when lipids are restricted.

Evidence: Further research needed

Recommendation: No recommendation

Fat emulsion with soy oil, medium-chain triglycerides, olive oil, and fish oil (SMOF) is not available in the United States. Until it is approved for use, no recommendation can be made for use in the United States. If available, the evidence supporting the use of SMOF for the treatment of cholestasis is very low quality. The randomized control trials (RCTs) are primarily safety and efficacy studies in preterm infants with the primary outcome of plasma phospholipid profiles and adverse events.

Evidence: Further research needed

Recommendation: No recommendation

Fat emulsions that contain a blend of refined olive and soybean oil have been approved for adults receiving parenteral nutrition (PN). It is not approved for infants or children. Until it is approved for use in children, no recommendation can be made for use in the United States.

Can Enteral Ursodeoxycholic Acid (UDCA) Improve the Treatment of PNALD in Pediatric Patients with Intestinal Failure?

A suggestion is made to use UDCA for the treatment of elevated liver enzymes in children with PNALD. The evidence is of very low quality and confounded with the presence of enteral feeding in conjunction with treatment with UDCA. In addition, the patients studied tend to be premature infants with an intact intestinal tract; therefore, the efficacy of UDCA may not be generalizable to patients with established intestinal failure. In the included studies, no harm from this treatment was reported. The desirable effect of the reduction of liver indices has to be weighed against the unknown efficacy of the treatment and the fact that in most cases, the study participants did not have primary intestinal pathology.

Evidence: Very low

Recommendation: Weak

Are PNALD Outcomes Improved When Patients Are Managed by a Multidisciplinary Intestinal Rehabilitation Team?

A suggestion is made to refer patients with PN-dependent intestinal failure to multidisciplinary intestinal rehabilitation programs. The evidence on this topic is of very low quality, but the improvement in survival is compelling, and the risk to the child of treatment with multidisciplinary practice is not increased.

Evidence: Very low

Recommendation: Weak

Definitions:

Note: The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) clinical guidelines have adopted concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group. A full description of the methodology is outlined in the A.S.P.E.N. guideline "Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients: applying the GRADE system to development of A.S.P.E.N. clinical guidelines" (see the "Availability of Companion Documents" field).

Quality of Evidence

High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.

Very Low	Any estimate of effect is very uncertain.

Strength of Recommendation

Strong	Net benefits outweigh harms
Weak	Tradeoffs for patient are important
Further research needed	Uncertain tradeoffs

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Parenteral nutrition–dependent intestinal failure
- Parenteral nutrition–associated liver disease (PNALD)

Guideline Category

Prevention

Treatment

Clinical Specialty

Critical Care

Gastroenterology

Nutrition

Pediatrics

Intended Users

Advanced Practice Nurses

Dietitians

Hospitals

Nurses

Pharmacists

Physician Assistants

Physicians

Guideline Objective(s)

To develop recommendations for the care of children with parenteral nutrition–dependent intestinal failure that have the potential to prevent parenteral nutrition–associated liver disease (PNALD) or improve its treatment

Target Population

Pediatric patients with intestinal failure who have or who are at risk of having parenteral nutrition–associated liver disease (PNALD)

Interventions and Practices Considered

1. Use of ethanol lock
2. Use of a reduced dose of soy-based fat emulsion (SOE)
3. Use of enteral ursodeoxycholic acid (UDCA)
4. Management by a multidisciplinary intestinal rehabilitation team

Note: The following interventions were considered but no recommendation was made:

Use of fish oil emulsion (FOE)
Use of fat emulsion with soy oil, medium-chain triglycerides, olive oil, and fish oil (SMOF)
Use of fat emulsions that contain a blend of refined olive and soybean oil

Major Outcomes Considered

- Incidence of catheter-related bloodstream infections (CLABSI)
- Incidence of central venous catheter replacements
- Risk of parenteral nutrition–associated liver disease (PNALD)
- Incidence of cholestasis
- Lipid profile and bilirubin and liver enzyme levels
- Incidence of essential fatty acid deficiency
- Feeding tolerance (days to full enteral feeds)
- Growth
- Overall survival
- Mortality
- Sepsis episodes

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

For the current Clinical Guideline, the following terms were used to search PubMed and CINAHL until May 2013: intestinal failure, short bowel syndrome, clinical outcomes, lipid, bloodstream infection, team, multidisciplinary team, parenteral nutrition, and enteral nutrition. The searches were limited to studies that included pediatric subjects, English-language publications, randomized controlled trials (RCTs), controlled observational studies, and uncontrolled case series.

Number of Source Documents

A total of 16 randomized controlled trials, 13 controlled observational studies, and 23 uncontrolled case series met the inclusion criteria and were abstracted.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Note: The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) clinical guidelines have adopted concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group. A full description of the methodology is outlined in the A.S.P.E.N. guideline "Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients: applying the GRADE system to development of A.S.P.E.N. clinical guidelines" (see the "Availability of Companion Documents" field).

Quality of Evidence

High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

A systematic review of the best available evidence to answer a series of questions regarding clinical management of children with intestinal failure receiving parenteral or enteral nutrition was undertaken and evaluated using concepts adopted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

These Clinical Guidelines were developed under the guidance of the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Board of Directors.

The A.S.P.E.N. Clinical Guidelines process has adopted concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group. A full description of the methodology has been published (see the "Availability of Companion Documents" field). Briefly, specific clinical questions where nutrition support is a relevant mode of therapy are developed and key clinical outcomes are identified. A rigorous search of the published literature is conducted, and each included study is assessed for research quality, tables of findings are developed, and the body of evidence for the question is evaluated. A recommendation for clinical practice that is based on both the best available evidence and the risks and benefits to patients is developed by consensus. Strong recommendations are made when the evidence is graded high and/or net

benefits outweigh harms. Weak recommendations are made when evidence is graded low or if there are important trade-offs to the patient. When limited research is available to answer a question, no recommendation can be made.

Rating Scheme for the Strength of the Recommendations

Note: The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) clinical guidelines have adopted concepts of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group. A full description of the methodology is outlined in the A.S.P.E.N. guideline "Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients: applying the GRADE system to development of A.S.P.E.N. clinical guidelines" (see the "Availability of Companion Documents" field).

Strength of Recommendation

Strong	Net benefits outweigh harms
Weak	Tradeoffs for patient are important
Further research needed	Uncertain tradeoffs

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Clinical Guidelines undergo peer review by clinical content experts both internal and external to the organization. The author and reviewer teams for this guideline include members of each of the professional groups that could play a role in the use of such a guideline (dietetics, nursing, medicine, pharmacy, research), as well as by the A.S.P.E.N. Board of Directors. After the author response to the initial reviews, the guideline was reviewed and approved by the A.S.P.E.N. Board of Directors and their legal consultant.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate support of pediatric patients with intestinal failure at risk of parenteral nutrition–associated liver disease

Potential Harms

- With ethanol lock, the desirable effect of both decreased infection and catheter removal has to be interpreted in light of the unknown effects of increased thrombus formation and disruption of catheter structure integrity.
- With soy-based fat emulsions (SOE), the desirable effect of reduction of liver indices has to be considered in light of the unknown effects of poor growth and development when lipids are restricted.

Qualifying Statements

Qualifying Statements

These American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) Clinical Guidelines are based on general conclusions of health professionals who, in developing such guidelines, have balanced potential benefits to be derived from a particular mode of medical therapy against certain risks inherent with such therapy. However, the professional judgment of the attending health professional is the primary component of quality medical care. Since guidelines cannot account for every variation in circumstances, the practitioner must always exercise professional judgment in their application. These Clinical Guidelines are intended to supplement, but not replace, professional training and judgment.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Safety

Identifying Information and Availability

Bibliographic Source(s)

Wales PW, Allen N, Worthington P, George D, Compher C, American Society for Parenteral and Enteral Nutrition, Teitelbaum D. A.S.P.E.N. clinical guidelines: support of pediatric patients with intestinal failure at risk of parenteral nutrition-associated liver disease. JPEN J Parenter Enteral Nutr. 2014 Jul;38(5):538-57. [71 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2014 Jul

Guideline Developer(s)

American Society for Parenteral and Enteral Nutrition - Professional Association

Source(s) of Funding

American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

Guideline Committee

Not stated

Composition of Group That Authored the Guideline

Authors: Paul W. Wales, MD; Nancy Allen, MLS, RD, CNSC; Patricia Worthington, MSN, RN; Donald George, MD; Charlene Compher, PhD, RD, CNSC, LDN, FADA, FASPEN; the American Society for Parenteral and Enteral Nutrition; Daniel Teitelbaum, MD

Financial Disclosures/Conflicts of Interest

Financial disclosure: None declared.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the Journal of Parenteral and Enteral Nutrition Web site .

Availability of Companion Documents

The following is available:

- Clinical guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients: applying the GRADE system to development of A.S.P.E.N. clinical guidelines. American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.); 2012 Jan. 5 p. Electronic copies: Available from the Journal of Parenteral and Enteral Nutrition Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on July 28, 2014. The information was verified by the guideline developer on August 22, 2014.

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